UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/991,262	11/20/2001	Peter Daniel Christian	A-58631-5/RFT/DJM	4471

7590 01/30/2004

RICHARD F. TRECARTIN, ESQ.
FLEHR HOHBACH TEST ALBRITTON & HERBERT LLP
Four Embarcadero Center, Suite 3400
San Francisco, CA 94111-4187

EXAMINER	
MEHTA, ASHWIN D	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 01/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/991,262	CHRISTIAN ET AL.	
	Examiner	Art Unit	
	Ashwin Mehta	1638	

-- The MAILING DATE f this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10,13,19,20,25-28,30,31,37 and 38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10,19,25-28,31,37 and 38* is/are rejected.

7)☒ Claim(s) *13,20 and 30* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 November 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

However, see item 2, pages 3-5.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4012002*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 10, 13, 19, 20, 25, 26, 30, 31 37, and 38, and SEQ ID NO: 47, in the paper filed October 30, 2003 is acknowledged. Applicant acknowledges that if claims 10, 25, and 26 are allowed, then the claims of non-elected Group II will be rejoined and examined (response, page 1, 2nd full paragraph). However, it was determined during the course of examination that it would not be an undue burden to further examine claims 27 and 28. Therefore, the claims of Groups I and II have been rejoined. All pending claims have been examined in this Office action.

Applicant traverses the requirement of election of a single nucleotide sequence for examination. Applicant argues that SEQ ID NOs: 47 and 50 both encode a *Helicoverpa armigera* Stunt Virus coat protein, and should be examined together (response, page 1, 3rd full paragraph). Applicant further asserts that it is proper for the Examiner to examine all of the nucleotide sequences of claim 10 together. Applicant argues that SEQ ID NOs: 39 and 47 were examined together in parent application 09/234,238, and that the Examiner would not be subject to an undue burden, as the searches in the previous application could be consulted (response, page 1, 4th full paragraph). Applicant's argument was found persuasive, and the nucleotide sequences recited in claim 10 have been rejoined and examined in this Office action.

Applicant also requested clarification on the request to further elect a nucleotide sequence from claim 13 if Group II was elected, because claim 13 was included in Group I, not Group II

(response, paragraph bridging pages 1-2). A further election by Applicant for a nucleotide sequence in claim 13 is not required. As the nucleotide sequences in claim 10 encode the *H. armigera* Stunt Virus replicase and capsid precursor, the only nucleotide sequences in claim 13 that will be examined are those that encode SEQ ID NOs: 40 and 50.

The requirement to restrict nucleotide sequences encoding the other proteins recited in claim 13 is still deemed proper and is therefore made FINAL. Non-elected subject matter in claims 13 and 30 (which recites plasmids that do not comprise nucleotide sequences encoding SEQ ID NOs: 40 or 50, or which do not comprise SEQ ID NO: 39 or SEQ ID NO: 47) should be deleted.

Priority

2. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119/120 as follows:

It is noted that this application appears to claim subject matter disclosed in prior Application No. 09/234,238, filed 1/20/1999, and 08/440,522, filed 5/12/1995. A reference to the prior application must be inserted as the first sentence of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e) or 120. See 37 CFR 1.78(a). For benefit claims under 35 U.S.C. 120, the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of all nonprovisional applications. Also, the current status of all nonprovisional parent applications referenced should be included.

If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference to the prior application must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification of in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number. It is noted that Applicant filed a preliminary amendment that inserted a statement the claimed priority to application 09/234,238. However, this statement does not mention application 08/440,522. Applicant should amend this statement to include 08/440,522, the relationship of the prior applications, and their status (they are both abandoned).

Specification

3. The specification fails to comply with the sequence rules of 37 CFR 1.821-1.825. The brief descriptions of Figures 2 and 3 should identify the amino acid sequences in those figures with their sequence identifiers. Correction is required.

4. The brief description of Figure 4 is objected to because it does not refer to the different parts of the figure. See 37 CFR 1.74. Correction is required.

Claim Objections

5. Claims 13, 20, and 30 are objected to for encompassing non-elected inventions (sequences).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 10, 19, 25-28, 31, and 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 10: the recitations, "a nucleotide sequence set forth in SEQ ID NO: 39", and "a nucleotide sequence set forth in SEQ ID NO: 47" (emphases added) in lines 3 and 4 render the claim indefinite. It is not clear if the recitations are referring to subsequences of the sequences set forth in SEQ ID NOs: 39 and 47, or the two sequences as a whole. If the recitations are referring to subsequences, it is not clear what subsequences are being referred to. It is suggested that the article, "a" in the recitations be replaced with --the--.

In claim 25: the recitation, "expresses or encapsidates" in line 2 renders the claim indefinite. The claim does not clearly indicate what the vector expresses or encapsidates.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 10, 19, 25-28, 31, 37, and 38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter

which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn towards any isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of: a) SEQ ID NO: 39, b) SEQ ID NO: 47, c) sequences encoding the amino acid sequence of SEQ ID NO: 40 or a replicase-encoding fragment thereof, d) sequences encoding the amino acid sequence of SEQ ID NO: 50 or a coat-protein encoding fragment thereof, e) a sequence having at least 90% identity to a) and which encode any replicase, f) sequences having at least 90% identity to b) and encoding any coat protein, g) sequences encoding any replicase which shares at least 90% amino acid sequence identity with SEQ ID NO: 40, and h) sequences encoding any coat protein which shares at least 90% identity with SEQ ID NO: 50; expression or transfer vectors comprising said molecule, or wherein said vectors comprise a ribozyme; plant host cells comprising said vector; transgenic plants comprising at least one of said molecules; and method of controlling insect attack in a plant comprising inserting into the plant a first nucleic acid selected from a) SEQ ID NO: 39, b) sequences encoding the amino acid sequence of SEQ ID NO: 40 or a replicase-encoding fragment thereof, c) a sequence having at least 90% identity to a) and which encode any replicase, and d) sequences encoding any replicase which shares at least 90% amino acid sequence identity with SEQ ID NO: 4; and a second nucleic acid selected from the group consisting of e) SEQ ID NO: 47, f) sequences encoding the amino acid sequence of SEQ ID NO: 50 or a coat-protein encoding fragment thereof, g) sequences having at least 90% identity to b)

and encoding any coat protein, and h) sequences encoding any coat protein which shares at least 90% identity with SEQ ID NO: 50, wherein the plant produces HaSV viral particles.

The specification teaches that *Heliocoverpa armigera* Stunt Virus (HaSV) is an insect virus that stunts the growth of insect larvae, for example that of *H. armigera*, by inhibiting or preventing development to the adult stage. The HaSV genome comprises two single-stranded, positive-sense RNAs. RNA1 (SEQ ID NO: 39) has 5310 nucleotides, and encodes a protein of 187 kD regarded as the RNA-dependent RNA polymerase (replicase; SEQ ID NO: 40). The open reading frame of the replicase spans nucleotides 34-5290 of SEQ ID NO: 39. The 3' end of RNA1 also encodes three small proteins, P11a (SEQ ID NO: 42), P11b (SEQ ID NO: 44), and P14 (SEQ ID NO: 46). RNA2 comprises 2470 nucleotides (SEQ ID NO: 47) and encodes a 71 kD polypeptide comprising two virus capsid proteins. This 71 kD peptide was therefore determined to be the capsid protein precursor, P71 (SEQ ID NO: 50), which is proteolytically cleaved to form the two capsid proteins. The open reading frame of P71 spans nucleotides 366 to 2309 of SEQ ID NO: 47. Another major translation product encoded by RNA2 has an apparent molecular weight of 24 kD, though the predicted molecular weight from the reading frame is 17 kD. The reading frame overlaps with that of the capsid precursor. This translation product is termed "P17," (SEQ ID NO 48) and is speculated as having a function in modifying or manipulating the growth characteristics or cell cycle of HaSV-infected insect cells (page 7; page 36, lines 25 to page 37, line 18; page 37, line 29 to page 40, line 25).

A review of the full content of the specification indicates that the nucleotide sequences set forth in SEQ ID NO: 39, SEQ ID NO: 47, and the amino acid sequences set forth in SEQ ID NO: 40 and SEQ ID NO: 50, are essential to the operation and function of the claimed invention.

A search for the sequences of SEQ ID NOs: 39, 40, 47, and 50 indicates that they are novel and unobvious.

A review of the language of claim 10 indicates that it is drawn to SEQ ID NO: 39, SEQ ID NO: 47, the genus comprising all nucleotide sequences that encode SEQ ID NO: 40 or any replicase-encoding fragment thereof, nucleotide sequences having at least 90% identity to SEQ ID NO: 39 and which encode a replicase, and nucleotide sequences that encode any replicase and which share at least 90% amino acid sequence identity with SEQ ID NO: 40; and the genus comprising nucleotide sequences encoding SEQ ID NO: 50 or any coat-protein-encoding fragment thereof, nucleotide sequences having at least 90% identity to SEQ ID NO: 47 and which encode a coat protein, nucleotide sequences that encode any coat protein and which share at least 90% amino acid sequence identity with SEQ ID NO: 50. The method of claim 37 uses the same nucleotide sequences as starting material.

However, the specification does not describe a single species of nucleotide sequences that encodes a fragment of SEQ ID NO: 40 that has replicase activity, or of nucleotide sequences that encodes a fragment of SEQ ID NO: 50 that has the activity of a coat protein, or of nucleotide sequences that have at least 90% identity SEQ ID NOs: 39 or 47 and that encode a replicase or coat protein, respectively (other than SEQ ID NOs: 39 and 47 and sequences that differ due to genetic code degeneracy), or of nucleotide sequences that encode a replicase or coat protein and which share at least 90% amino acid sequence identity to SEQ ID NO: 40 or 50, respectively.

The Federal Circuit provided the appropriate standard for written description in *University of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997). The court held that a structural description of a rat cDNA was not an adequate description of broader

classes of cDNAs, because a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." The court also held in *Lilly* that a genus of cDNAs could be described by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.

In the instant application, the specification does not describe the structural features of the replicase of SEQ ID NO: 40 that are essential to its activity. The specification indicates that SEQ ID NO: 40 is "thought" to encode an RNA-dependent RNA polymerase (replicase) because it contains a conserved Gly-Asp-Asp sequence and "surrounding sequences" that are in replicases, in addition to "further homology" encoded by the polymerase of tobacco mosaic virus and other plus-stranded RNA viruses (page 37, lines 5-11). However, this is insufficient to describe fragments of SEQ ID NO: 40 that retain its replicase activity, or of nucleotide sequences that differ from SEQ ID NO: 39 by as much as 10%, do not encode SEQ ID NO: 40 and which still encode a replicase that acts on the HaSV genome, or of nucleotide sequences that encode a replicase that acts on the HaSV genome and which can differ from SEQ ID NO: 40 by as much as 10%. The "surrounding sequences" and "further homology" that are supposedly shared by SEQ ID NO: 40 and the replicases of tobacco mosaic virus and other plus-stranded RNA viruses are not described. Further, tobacco mosaic virus is a plant virus, not an insect virus. Evidence is lacking in the specification or the prior art showing that a plant virus replicase, or a non-HaSV replicase, can act as a replicase for the HaSV genome, despite having some sequences in

common. Bawden et al. (J. Invert. Pathol., 1999, Vol. 74, pages 156-163) teach that while insect viruses of the Nodaviradae family are structurally similar to the Tetraviridae (of which HaSV is member), the similarity is not reflected in their ability to replicate outside of specific insect cells. Nodaviruses can replicate in a wide variety of cell types, whereas HaSV can only replicate in specific tissue within lepidopteran insect hosts (page 162). This indicates that the presence of common structures between the replicases of HaSV and other viruses is not a determinant of functional activity. Other structural features of SEQ ID NO: 40 that are essential to its particular functional activity are not described. In the absence of this information, one skilled in the art would not identify fragments of SEQ ID NO: 40, or the nucleotide sequences encoding them, that retain HaSV replicase function, or nucleotides sequences that encode amino acid sequences that differ from SEQ ID NO: 40 and which retains its functional activity.

The specification also does not describe the structural features of the HaSV coat protein precursor, SEQ ID NO: 50, which are essential to its function. The specification does not describe the amino acid residues of SEQ ID NO: 50 that can be deleted or changed, without affecting its function. Since the specification describes no structural features that are common to the members of the genus, it necessarily does not describe structural features that constitute a substantial portion of the genus. The specification does not describe a single nucleotide sequence that encodes a fragment of SEQ ID NO: 50, or which encodes a protein that differs from SEQ ID NO: 50, and which retains its function as a coat protein precursor of HaSV. Further, regarding parts d), f), and h) of claim 10 and parts f)-h) of claim 37: SEQ ID NO: 47 encodes a coat protein precursor, SEQ ID NO: 50. As discussed above, HaSV has two capsid proteins, not one. Yet, parts d), f), and h) of claim 10 and parts f)-h) of claim 37 indicate that the

nucleotide sequence encodes a coat protein. The specification provides no description of changes that can be made to SEQ ID NO: 47 or SEQ ID NO: 50 such that only one coat protein can function in the formation of HaSV particles.

Further, it is noted that claim 10 does not contain any limitation that the amino acid sequences encoding by the nucleotide sequences of parts c)-h) must function with the HaSV genome. The specification does not describe any nucleotide sequences encoding replicases or coat proteins as indicated in the claim that can function with other viruses. Given the breadth of the claims and the description in the specification of only nucleotide sequences encoding SEQ ID NO: 40 and SEQ ID NO: 50, and the nucleotide sequences of SEQ ID NO: 39 and SEQ ID NO: 47, it is submitted that the specification fails to provide an adequate written description of the multitude of nucleotide sequences encompassed by the claims.

8. Claims 10, 19, 25-28, 31, 37, and 38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO: 39, SEQ ID NO: 47, nucleotide sequences encoding SEQ ID NO: 40 and SEQ ID NO: 50, and a method of controlling insect attack of a plant comprising inserting into a plant a first nucleic acid encoding SEQ ID NO: 40 and a second nucleic acid encoding SEQ ID NO: 50, wherein the nucleic acid molecules also comprise a ribozyme, does not reasonably provide enablement for nucleotide sequences that encode fragments of SEQ ID NO: 40 or SEQ ID NO: 50 that encode replicases or a coat protein, respectively, or nucleotide sequences that encode amino acid sequences the differ from SEQ ID NO: 40 or SEQ ID NO: 50 and encode replicases or a coat protein, a method of controlling insect attack of a plant comprising inserting first and second nucleic acids encoding SEQ ID NO: 40

and SEQ ID NO: 50 that do not also encode a ribozyme, or transgenic plants that do not comprise SEQ ID NO: 39 and nucleotide sequence encoding SEQ ID NO: 50. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

As discussed above, the specification teaches the nucleotide sequences of RNA1 and RNA2 of HaSV. RNA1 (SEQ ID NO: 39) has 5310 nucleotides, and encodes a protein of 187 kD regarded as the RNA-dependent RNA polymerase (replicase; SEQ ID NO: 40). The open reading frame of the replicase spans nucleotides 34-5290 of SEQ ID NO: 39. The 3' end of RNA1 also encodes three small proteins, P11a (SEQ ID NO: 42), P11b (SEQ ID NO: 44), and P14 (SEQ ID NO: 46). RNA2 comprises 2470 nucleotides (SEQ ID NO: 47) and encodes a 71 kD polypeptide comprising two virus capsid proteins. This 71 kD peptide was therefore determined to be the capsid protein precursor, P71 (SEQ ID NO: 50), which is proteolytically cleaved to form the two capsid proteins. The open reading frame of P71 spans nucleotides 366 to 2309 of SEQ ID NO: 47. Another major translation product encoded by RNA2 has an apparent molecular weight of 24 kD, though the predicted molecular weight from the reading frame is 17 kD. The reading frame overlaps with that of the capsid precursor. This translation product is termed "P17," (SEQ ID NO 48) and is speculated as having a function in modifying or manipulating the growth characteristics or cell cycle of HaSV-infected insect cells.

The specification also teaches that HaSV RNA and virus electroporated into *Nicotiana plumbaginifolia* protoplasts resulted in replication (page 63, lines 5-19). It is noted, however, that Gordon et al. (Virology, 2001, Vol. 288, pages 36-50) also teach that replication of HaSV RNA could not be detected in *N. plumbaginifolia* protoplasts that had been electroporated with

HaSV genomic RNA, and conclude that replication is not involved in the HaSV viral assembly process (page 39). The specification teaches that bioassays were conducted in which *N. plumbaginifolia* and oat protoplasts comprising the HaSV RNA was fed to neonate *H. armigera* larvae. Significant stunting of the larvae was observed (pages 63-64). Expression plasmids comprising cDNAs of RNA1 or RNA2 also comprise cis-acting ribozymes. Virus replication is not observed in the absence of these ribozymes (paragraph bridging pages 64-65). For plant transformation, the cDNAs were placed under the control of the CaMV 35S promoter. The ribozyme and a polyadenylation signal follow the cDNA on the plasmid (page 79, line 1 to page 81, line 5). Plasmids comprising the cDNA of RNA1 or RNA2 were transfected by electroporation into *N. plumbaginifolia* protoplasts, and fed to heliothis larvae. Stunting was observed only in those larvae that fed on protoplasts comprising both RNA1 and RNA2, and then only if the plasmid also contained a ribozyme. Expression of RNA1 or RNA1 alone in the protoplasts did not lead to assembly of infectious particles (page 81, lines 8 to page 83, line 21). Agrobacterium binary vectors comprising the cDNA of RNA1 and RNA2, RNA1 and RNA2 and coding sequence of the capsid precursor, RNA1 and the coding sequence of the capsid precursor, or RNA2 alone, were also prepared for production of transgenic plants. The vectors also comprised the sequence of the ribozyme, after the cDNAs. Nicotiana tabacum leaf discs were transformed via Agrobacterium, and transgenic plants regenerated. Leaves from the plants were separated and fed to neonate heliothis larvae. The leaves from plants comprising plasmids expressing RNA1 and RNA2, or RNA1 and the sequence for the capsid precursor, showed less leaf damage versus control leaves, and larvae feeding on those leaves weighed less than those feeding on leaves from control plants (page 86, line 10 to page 91, line 9).

A review of the language of claim 10 indicates that it is drawn to SEQ ID NO: 39, SEQ ID NO: 47, the genus comprising all nucleotide sequences that encode SEQ ID NO: 40 or any replicase-encoding fragment thereof, nucleotide sequences having at least 90% identity to SEQ ID NO: 39 and which encode a replicase, and nucleotide sequences that encode any replicase and which share at least 90% amino acid sequence identity with SEQ ID NO: 40; and the genus comprising nucleotide sequences encoding SEQ ID NO: 50 or any coat-protein-encoding fragment thereof, nucleotide sequences having at least 90% identity to SEQ ID NO: 47 and which encode a coat protein, nucleotide sequences that encode any coat protein and which share at least 90% amino acid sequence identity with SEQ ID NO: 50. The method of claim 37 requires the same nucleotide sequences as starting material.

However, the specification does not teach any nucleotide sequences that encode a fragment of SEQ ID NO: 40 that has replicase activity, or nucleotide sequences that encode a fragment of SEQ ID NO: 50 that has the activity of a coat protein, or nucleotide sequences that have at least 90% identity SEQ ID NOs: 39 or 47 and that encode a replicase or coat protein, respectively (other than SEQ ID NOs: 39 and 47 and sequences that differ due to genetic code degeneracy), or nucleotide sequences that encode a replicase or coat protein and which share at least 90% amino acid sequence identity to SEQ ID NO: 40 or 50, respectively. The specification does not teach how the nucleotide sequences of SEQ ID NOs: 39 or 47, or the amino acid sequences of SEQ ID NOs: 40 or 50, may be altered without affecting their functional activity. As discussed above, Bawden et al. teach that the replicases of Nodaviradae insect viruses are structurally similar to that of HaSV, but that this similarity is not reflected in their ability to replicate outside of specific insect cells. Nodaviruses can replicate in a wide variety of cell

types, whereas HaSV can only replicate in specific tissue within lepidopteran insect hosts (page 162). Other structural features of SEQ ID NO: 40 that are essential to its particular functional activity are not described. While the specification indicates that the HaSV replicase contains a conserved GDD triplicate that is common to the replicases, this structure apparently is not sufficient to account for the specificity of the HaSV replicase. In the absence of this information, undue experimentation would be required by one skilled in the art to determine what portions of SEQ ID NO: 39, can be deleted or altered such that the encoded amino acid sequences retains HaSV replicase function.

The specification also does not teach structural features of SEQ ID NO: 50 that are common to the members of the genus, and which are required for its function as a HaSV capsid precursor. The specification does not teach a single nucleotide sequence that encodes a fragment of SEQ ID NO: 50, or which encodes an amino acid sequence that differs from SEQ ID NO: 50, and which retains its function as a coat protein precursor of HaSV. Bawden et al. teach that the capsids of HaSV and Nodaviradae show a distinct structural relationship, but have different symmetries (page 162). The structural domains of SEQ ID NO: 50 that account for the specificity of HaSV are not taught by the specification. In the absence of this information, undue experimentation would be required by one skilled in the art to determine the nucleotide sequences of SEQ ID NO: 47, or the amino acid sequences of SEQ ID NO 50, that can be altered or deleted without altering its function.

A review of the language of claim 37 indicates that the first and second nucleic acids need not comprise a ribozyme operably linked to the nucleotide sequences encoding the HaSV replicase and capsid precursor. However, the specification indicates that the presence of the

ribozyme is essential. As discussed above, the specification teaches that the plasmids used in the construction of transgenic plants contained a ribozyme. Further, the specification also teaches that protoplasts transfected with HaSV RNA1 and RNA2 alone, in the absence of the ribozymes, did not lead to the assembly of infectious HaSV particles (page 81, lines 15-26). Given the guidance in the specification, one skilled in the art would not be able to practice the claimed method of controlling insect attack of a plant if the nucleic acid molecules comprising the HaSV replicase and capsid precursor coding sequences were not operably linked to a ribozyme.

Further, regarding claim 38: the claim encompasses transgenic plants that can comprise only one of the nucleic molecules of claim 10. However, the specification does not teach how one skilled in the art is to use such a plant. As discussed above, the only transgenic plants that slowed the growth of H. armigera larvae and which showed less leaf damage caused by H. armigera larvae were those that expressed both the HaSV replicase and coat protein precursor. The specification does not teach any other use for transgenic plants that express only the replicase or the capsid precursor. Uses for such plants are also not evident from the teachings of the prior art. See Genentech, Inc. V. Novo Nordisk, A/S, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention. Given the breadth of the claims, unpredictability of the art, and lack of guidance of the specification as discussed above, undue experimentation would be required by one skilled in the art to make and use the claimed invention.

9. Claims 10, 13, 19, 20, 25-28, 30, 31, 37, and 38 are deemed free of the prior art, given the failure of the prior art to teach or fairly suggest SEQ ID NO: 39, SEQ ID NO: 47, and nucleotide sequences encoding SEQ ID NOs: 40 or 50.

10. Claims 13, 20, and 30 are objected, and claims 10, 19, 25-28, 31, 37, and 38 are rejected.

Contact Information

Any inquiry concerning this or earlier communications from the examiner should be directed to Ashwin Mehta, whose telephone number is 571-272-0803. The examiner can normally be reached on Mondays-Thursdays and alternate Fridays from 8:00 A.M to 5:30 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at 571-272-0804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 and 703-872-9306 for regular communications and 703-872-9307 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

January 20, 2004

Ashwin D. Mehta, Ph.D.
Primary Examiner
Art Unit 1638